

WHAT IS CLAIMED IS:

1. A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

- 5 (a) providing an assay system comprising a MAP2K6 polypeptide or nucleic acid;
 (b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and
 (c) detecting a test agent-biased activity of the assay system, wherein a difference
10 between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent.

2. The method of Claim 1 wherein the assay system includes a screening assay comprising a MAP2K6 polypeptide, and the candidate test agent is a small molecule modulator.

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3. The method of Claim 2 wherein the screening assay is a kinase assay.

4. The method of Claim 1 wherein the assay system includes a binding assay comprising a MAP2K6 polypeptide and the candidate test agent is an antibody.

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5. The method of Claim 1 wherein the assay system includes an expression assay comprising a MAP2K6 nucleic acid and the candidate test agent is a nucleic acid modulator.

25 6. The method of Claim 5 wherein the nucleic acid modulator is an antisense oligomer.

7. The method of Claim 6 wherein the nucleic acid modulator is a PMO.

8. The method of Claim 1 wherein the assay system comprises cultured cells or a non-human animal expressing MAP2K6,

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and wherein the assay system includes an assay that detects an agent-biased change in branching morphogenesis

9. The method of Claim 8 wherein the branching morphogenesis is angiogenesis.

10. The method of Claim 8 wherein the assay system comprises cultured cells.

11. The method of Claim 10 wherein the assay detects an event selected from the group consisting of cell proliferation, cell cycling, apoptosis, tubulogenesis, cell migration, cell sprouting and response to hypoxic conditions.

12. The method of Claim 10 wherein the assay detects tubulogenesis or cell migration or cell sprouting, and wherein the assay system comprises the step of testing the cellular response to stimulation with at least two different pro-angiogenic agents.

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13. The method of Claim 10 wherein the assay detects tubulogenesis or cell migration, and wherein cells are stimulated with an inflammatory angiogenic agent.

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14. The method of Claim 8 wherein the assay system comprises a non-human animal.

15. The method of Claim 14 wherein the assay system includes a matrix implant assay, a xenograft assay, a hollow fiber assay, or a transgenic tumor assay.

16. The method of Claim 15 wherein the assay system includes a transgenic tumor assay that includes a mouse comprising a RIP1-Tag2 transgene.

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17. The method of Claim 1, comprising the additional steps of:

(d) providing a second assay system comprising cultured cells or a non-human animal expressing MAP2K6 ,

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(e) contacting the second assay system with the test agent of (b) or an agent derived therefrom under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity; and

(f) detecting an agent-biased activity of the second assay system,

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wherein a difference between the agent-biased activity and the reference activity of the second assay system confirms the test agent or agent derived therefrom as a candidate branching morphogenesis modulating agent,

and wherein the second assay system includes a second assay that detects an agent-biased change in an activity associated with branching morphogenesis.

18. The method of Claim 17 wherein second assay detects an agent-biased change in an activity associated with angiogenesis.

19. The method of Claim 17 wherein the second assay system comprises cultured cells.

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20. The method of Claim 19 wherein the second assay detects an event selected from the group consisting of cell proliferation, cell cycling, apoptosis, tubulogenesis, cell migration, cell sprouting and response to hypoxic conditions.

10 21. The method of Claim 20 wherein the second assay detects tubulogenesis or cell migration or cell sprouting, and wherein the second assay system comprises the step of testing the cellular response to stimulation with at least two different pro-angiogenic agents.

15 22. The method of Claim 20 wherein the assay detects tubulogenesis or cell migration, and wherein cells are stimulated with an inflammatory angiogenic agent.

23. The method of Claim 17 wherein the assay system comprises a non-human animal.

20 24. The method of Claim 23 wherein the assay system includes a matrix implant assay, a xenograft assay, a hollow fiber assay, or a transgenic tumor assay.

25. The method of Claim 24 wherein the assay system includes a transgenic tumor assay that includes a mouse comprising a RIP1-Tag2 transgene.

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26. A method of modulating branching morphogenesis in a mammalian cell comprising contacting the cell with an agent that specifically binds a MAP2K6 polypeptide or nucleic acid.

30 27. The method of Claim 26 wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with branching morphogenesis.

28. The method of Claim 26 wherein the agent is a small molecule modulator, a nucleic acid modulator, or an antibody.

29. The method of Claim 26 wherein the branching morphogenesis is angiogenesis

30. The method of Claim 29 wherein tumor cell proliferation is inhibited.

5 31. A method for diagnosing a disease in a patient comprising:

- (a) obtaining a biological sample from the patient;
- (b) contacting the sample with a probe for MBM expression;
- (c) comparing results from step (b) with a control; and
- (d) determining whether step (c) indicates a likelihood of disease.

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32. The method of Claim 31 wherein said disease is cancer.

33. The method according to Claim 32, wherein said cancer is a cancer as shown in Table 1 as having >25% expression level.

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